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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/634,363	08/09/2000	Kevin Pang	CIBT-P02-058	5665

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EXAMINER
DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
1647	19

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/634,363	PANG ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 40-58* is/are pending in the application.

4a) Of the above claim(s) *8-12 and 40-50* is/are withdrawn from consideration.

5)☒ Claim(s) *58* is/are allowed.

6)☒ Claim(s) *1-7 and 51-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-12 and 40-58* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152).
6) ☐ Other: .

Status of Application, Amendments and/or Claims

The amendment filed 27 June 2003 (Paper No. 17) has been entered in full. Claims 13-39 are cancelled. New claims 51-58 were added.

The Formal Drawings filed 13 August 2003 (Paper No. 18) have been entered.

Claims 1-7 and 51-58 are under examination.

Withdrawn Objections And/Or Rejections

The rejection of claims 1-7 under 35 USC 112, first paragraph as set forth at pages 3-5 of the previous Office Action (24 March 2003, Paper No. 16) is *withdrawn in part* in view of the amendment (27 June 2003, Paper No.17). Please see remaining scope of enablement issues below.

The rejection of claims 1-2 under 35 USC 102(b) as being anticipated by Bertrand *et al.,* Pancreas 7(5):595-600, 1992 as set forth at pages 7-8 of the previous Office Action (24 March 2003, Paper No. 16) is *withdrawn* in view of the amendment (27 June 2003, Paper No.17).

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants have addressed the rejections of claims 1-7 made under 35 USC 112, first paragraph, enablement, regarding a method for promoting the growth of pancreatic

cells and a method for reducing degeneration of pancreatic tissue (pages 3-5 the previous Office Action, 24 March 2003, Paper No. 16). Because claims 1-7 were amended and new claims 51-58 were added, the Examiner will address Applicants' argument as it applies to the current claims.

Claims 2-7, 51, 52, 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for maintaining the glucose-responsiveness of pancreatic cells, comprising contacting pancreatic cells with a composition comprising an amount of peptidyl peptide YY (PYY) effective to maintain glucose-responsiveness of pancreatic cells

does not reasonably provide enablement for:

a method for maintaining the glucose-responsiveness of pancreatic cells, comprising contacting pancreatic cells with a composition comprising an amount of **peptidyl peptide YY (PYY) agonist** effective to maintain glucose-responsiveness of pancreatic cells

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification fails to teach how to make PYY variants/derivatives or PYY agonists that would maintain the claimed activity (maintaining glucose-responsiveness of pancreatic cells). The instant claims recite PYY agonist and PYY agonist comprising a polypeptide at least 90% identical to SEQ ID NO:2 (PYY).

Applicants cite references to support the assertion that the art at the time of filing included a panoply of PYY agonists and one of ordinary skill in the art using assays described in these references could have identified any number of additional PYY agonists using only routine experimentation. Applicants state that a patent need not teach, and preferably omits, what is well known in the art. Applicants cite MPEP 2164.01(a). Applicants' arguments have been fully considered but not deemed persuasive. The references cited by Applicants are not drawn to methods of promoting maturation of glucose responsive or maintaining glucose-responsiveness of pancreatic cells. Thus Applicants' argument regarding what is well known in the art is incorrect because no previously known PYY agonists were known to have the activity required in the instant claims.

Applicants state that even if the claims encompass certain inoperative embodiments, that do not undermine the enablement of the operative subject matter. Applicants cite MPEP 2164.08(b) and In re Angstadt. Applicants contend that one of skill in the art can readily make and test PYY variants to identify variants which meet the structural and functional limitations recited in the claims without undue experimentation. Applicants remind the Examiner that several PYY variants had been identified and the ability of these variants to mimic one or more functions of PYY had been demonstrated.

Applicants' arguments have been fully considered but not deemed persuasive. The section cited by Applicants' further states that the standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally

required in the art. The section also states that the scope of the claim may still not be enabled where undue experimentation is involved in determining those embodiments that are operable. The specification does not teach how to make any variant of PYY while still maintaining the claimed activity. The disclosure provides no guidance as to which regions of the protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence which would be within the claims.

Undue experimentation is a conclusion reached by weighing all of the wands factor. If one skilled in the art can readily anticipate the effect, than there is predictability in the art. In this case, however, the art is unpredictable based on the evidence provided (i.e. sequence mutations). The evidence for the degree of predictability in the art also relates to the amount of direction needed in the specification. The instant claims encompass any chemical structure, biological equivalent and derivative/variant of PYY. No structural limitations are recited for "PYY agonists". Thus, an infinite number of compounds are to be screened for the recited activity. Without sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. A considerable amount of time is permissible for the quantity of experimentation needed to make or use the invention based on the disclosure. However this depends on if the invention is routine or if the skilled artisan is given sufficient direction or guidance. In the instant

case, the experimentation is not routine and Applicant has provided little or no guidance.

As was stated above, no previously known PYY variants were known to have the claimed activity in pancreatic cells. The evidence of record indicates that PYY can maintain glucose-responsiveness of pancreatic cells. No evidence has been submitted that any other PYY agonist has this activity. Thus the evidence of record does not support the breadth of the claims.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1, 53, 54 and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims recite a method for promoting maturation of glucose responsive pancreatic cells, comprising contacting pancreatic cells with a composition comprising an amount of peptidyl peptide YY (PYY) or PYY agonist effective to promote the maturation of glucose responsive pancreatic cells.

The specification has not taught maturation of glucose-responsive pancreatic cells in response to PYY or PYY agonist. While the specification does demonstrate glucose responsiveness of cells in culture upon administering PYY, this alone does not prove maturation. Pancreatic islets or cells express markers indicative of maturation. The specification fails to show that various assays were employed to show

morphological changes, expression of specific genes or surface markers that demonstrate maturation has taken place.

Due to the large quantity of experimentation necessary to demonstrate maturation of glucose responsive pancreatic cells in response to PYY or PYY agonists, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite limitations structural limitations for PYY agonists, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 1-7, 51-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pages 5-7 of the previous Office Action (24 March 2003, Paper No. 17).

Applicants traverse the rejection and maintain that it is moot in light of the amended claims. Applicants contend that the specification provides an adequate description for a wide range of PYY agonists including peptide and non-peptide agonists. Applicants contend that they have described the genus of PYY agonists for

use in the claimed methods using both structural and functional criteria, and thus one of skill in the art can readily envision the claimed subject matter.

Applicants' arguments have been fully considered but not deemed persuasive. The specification states that these types of changes are routinely done in the art. The specification, however, does not provide any guidance as to what specific changes should be made. Explicit, not general guidance is what is needed. There is no description of variants of PYY or PYY agonist that exist, while still maintaining the claimed function. No structural limitations are recited for "PYY agonist". Furthermore, the instant claims encompass sequences that have a recited degree of identity (similarity, homology), and so forth and undefined lowering of stringency before termination of hybridization. In the absence of a recitation of clear hybridization conditions, the nucleic acid probe will hybridize with unrelated DNA sequences, corresponding sequences from other species, mutated sequences, allelic variants, splice variants and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph.

The specification provides insufficient written description to support the genus encompassed by the claim. The disclosure fails to provide a representative number of species to describe the genus. Applicant's argument has failed to overcome the 35 USC 112, first paragraph written description rejection. As was stated in the last Office Action, several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be

conserved over biomolecules of related function upon a significant amount of further research.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 52, 53 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, 53 and 55 are indefinite because "stringent conditions including" allows for undefined lowering of stringency before termination of hybridization.

Claim 52 is indefinite because of the recitation "a polypeptide encodable by" as opposed to "the polypeptide encoded by". "A" begs the question of which one. There are 6 possible open reading frames. "Encodable" begs the question of what conditions are required so that SEQ ID NO:1 does, in fact, encode the polypeptide.

Conclusion

Claims 1-7, 51-57 are rejected.

Claim 58 is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
September 23, 2003

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER